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I. Prokhaska, I.V. Khavkina and Z.I. Barbasheva

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EFFECT OF PROLONGED HYPOKINESIA ON THE HEART MUSCLE OF RATS

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Thirty-forty day hypokinesia leads to a sharp reduction in body weight and heart weight, especially its right ventricle, in experimental animals. A weakening of the contractile power of the myocardium and its resistance to the stress effect of anoxia were found. In this case, a reduction in the rate of anaerobic metabolism was found: in the right ventricle, of glycolysis and glycogenolysis and in the left, of glycogenolysis. The glycogen content in the heart muscles of rats after 30-40 day hypokinesia was unchanged. /1237*

It is known that prolonged restriction of mobility reduces the general, nonspecific resistance of the body, the condition of its functional systems, as well as the efficiency of the body as a whole and of its tissues. Unfavorable changes are manifested here in the morphology of individual organs and in metabolism in the tissues [4, 8-11, 18]. However there is not a clear picture of the changes induced in body tissues under the influence of prolonged hypokinesia.

This work is devoted to study of the myocardium, as a muscle working continually under conditions of hypokinesia. Its efficiency, resistance to the stress effect of anoxia and anaerobic metabolism after 30-40 days of hypokinesia were investigated.

Method

Male, white Wistar rats, weighing 220-270 g, were used in the tests. The test animals were placed in individual

*Numbers in the margin indicate pagination in the foreign text.

plexiglass cells. The cell design eliminated the possibility of movement by the animals. Only the forepaws and head retained some mobility, providing for food intake. The control rats were kept in cages, ten to a cage. The feeding conditions and composition were identical for both groups of animals. The rats were decapitated for study of resistance of the myocardium and metabolism in it.

Myocardium resistance was determined on the isolated right ventricle, since the small thickness of this muscle permitted a constant flow of O_2 to it from the environment to be ensured. Under the conditions selected, the physiological excitability of the muscles was preserved for a long period of time (over 2 hours. Determination of the ability of the myocardium to recover the contractile function after 20 minute anoxia served as a criterion of myocardium resistance, in accordance with the method first developed by Kopetskiy [15] and improved by I. Prokhaska [16]. For this purpose, rhythmic electrical pulses, at a frequency of 60 pulses per minute, were supplied to the right ventricle, by means of platinum electrodes. In this case, the muscles were immersed in Krebs-Ringer solution pH 7.34 (temperature 34°), with continuous oxygen supply. The rhythmic contractions of the heart muscle in the isotonic mode were recorded by a kymograph. After establishment of a stable myocardium contraction amplitude, oxygen was replaced by nitrogen for 20 min. Anoxia induced a gradual weakening of the contractions of the myocardium, right up to their complete disappearance, in response to continuing stimulation. The nitrogen was replaced by oxygen after 20 min, after which the contractile function of the myocardium was gradually restored. After establishment of contraction amplitude at a stable level, always lower than before /1238 anoxia, the contraction amplitude was measured before and after anoxia, and the percentage ratio of the measured amplitudes was calculated. This value was the criterion of resistance of the

myocardium to anoxia. The height of the myogram alone served as a relative criterion of contraction strength for us.

For investigation of glycolytic metabolism in the myocardium, the isolated heart was placed in 0.44 M mannose at 0°. Homogenization of the ventricles was carried out in a homogenizer with a teflon pestle, in a medium of 0.44 M mannose, pH 7.4, for a period of 40-50 sec. The glycolysis and glycogenolysis rates were determined from accumulation of lactic acid in a system, which contained optimum concentrations of coenzymes and activators, in moles/ℓ: K-phosphate buffer $4 \cdot 10^{-2}$, pH 7.4; ATP $1 \cdot 10^{-3}$; NAD $2 \cdot 10^{-4}$; $MgCl_2$ $2 \cdot 10^{-3}$; fructose-1,6-diphosphate $8 \cdot 10^{-5}$. $4 \cdot 10^{-2}$ M glucose or 2 mg per sample glycogen served as substrates. Total sample volume was 1.25 ml. Incubation was carried out under argon for 30 min at 30°. Lactic acid was determined by the method of Barker and Sammerson, in the Ström modification [18]. Glycogen in the ventricles of the heart was determined by the method of Kemp [14], in tissue specimens frozen with liquid nitrogen.

Results of Investigation and Discussion

Change in Body Weight and Heart Weight under the Influence of Hypokinesia

It is clear from Table 1 that 30-40 days of hypokinesia (HK) led to a decrease in body weight of the animals. While a constant weight increase was noted in the control rats, amounting to 32% in 30-40 days, the body weight in HK animals amounted to only 93% of the initial level. As a result, the body weight of HK rats turned out to be 43% lower than in the control animals, which is evidence of an acute dystrophy in the HK animals. These data are in complete conformance with those in the literature [5, 10] and our previously published data [4].

TABLE 1. CHANGE IN BODY WEIGHT (g) AND HEART WEIGHT (mg) IN RATS AFTER 3 -40 DAYS OF HYPOKINESIA.

Animal Group	Body Weight		Heart	Right Ventricle	Left Ventricle	Index (Right/Left)
	Initial	After 30-40 days				
Control	208±9.1 (8)	274±7.0 (8)	820±32.2 (8)	194±7.3 (8)	420±17.5 (8)	0.46±0.02 (8)
Hypokinesia	207±8.9 (10)	192±9.1 (10)	636±28.4 (10)	142±7.5 (10)	351±19.3 (10)	0.40±0.03 (10)
P		<0.001	<0.001	<0.001	<0.05	Not significant

Note: Numbers in parentheses, number of animals examined.

The heart weight of HK rats also was reduced. It amounted to 69% of the control values. In this case, the weight of the left ventricle was 20%, and of the right, 36% lower than in the control animals. Nevertheless, the index weight of right/weight of left in HK rats practically did not differ from the control values. A small reduction of it in the HK animals was not statistically significant.

Contractile Power and Resistance of Myocardium

Individual values, characterizing the resistance of the right ventricle of the hearts of control and HK rats, are shown in Fig. 1. It is clear that, after 20-minute anoxia, the contractile function of the myocardium in HK animals recovered by only 58.3%, while it was 74.4% in the control animals. The reduction observed in resistance to anoxia apparently is evidence of deterioration of the functional condition of the myocardium.

Data characterizing the strength of contractions of the right ventricle of the hearts of rats expressed as a percentage of the contraction amplitude in HK rats to control values before and after anoxia, are presented in Table 2. It follows from the

Fig. 1. Extent of recovery of contractile function of right ventricle of the heart after 20-minute anoxia (in percent of initial): ordinate, percentage ratio of amplitude of contractions of myocardium after anoxia to initial values; open circles individual data for control rats; black circles after 30-40 day hypokinesia; vertical bars M ± m.

table that, both before and after anoxia, the strength of contraction of the cardiac muscles of HK rats was considerably less than in the contr l animals. It might be thought that the lesser extent of effort gene ted by the heart muscles of /1239 the rats is explained by their lower weight. However, the weight of the right ventricle in HK rats was less than in the controls by 36%, while the strength of its contractions was reduced by 44% before anoxia and b 56% after it. This difference gave us grounds for considering that hypokinesia leads precisely to weakening of the myocardium, to reduction in its ability tc generate effort.

TABLE 2. STRENGTH OF CONTRACTION OF ISOLATED RIGHT VENTRICLE OF HEART OF RAT BEFORE AND AFTER ANOXIA, IN PERCENT OF CONTROL.

Characteristic	Before Anoxia		After Anoxia	
	Control	Hypokinesia	Control	Hypokinesia
Strength of contraction	100(8)	54.4±5.1(10)	100(8)	43.8±5.1(10)

Note: numbers in parentheses, number of experimental animals.

We obtained similar data on the skeletal muscles of HK animals [6].

Anaerobic Metabolism

The data presented in Fig. 2 are evidence that, as a result of 30-40 days of restriction of mobility of an animal, a small decrease in the rate of anaerobic metabolism was noted. A reduction in the rates of both glycolysis and glycogenolysis took place in the right ventricle and only of glycogenolysis in the left one.

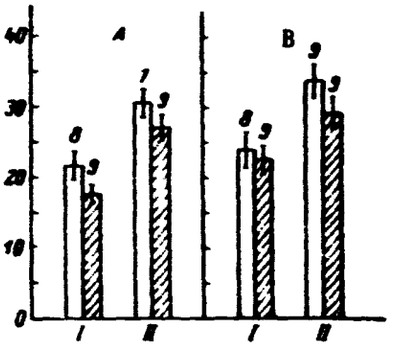

Fig. 2. Effect of 30-40 days of hypokinesia on rate of glycolysis (I) and glycogenolysis (II) in the right (A) and left (B) ventricles of the hearts of rats: ordinate, lactic acid accumulation, in μg/mg dry weight/hour; white columns control; cross-hatched ones, HK rats; numbers in columns, number of animals used.

Attention was turned to the fact that, under the influence of hypokinesia, the ratio of the glycolysis and glycogenolysis rates changed in the myocardiums of the animals. Thus, the glycogenolysis rate exceeded the glycolysis rate by approximately 40% in the right and left ventricles normally. After a month of hypokinesia of the rats, this value amounted to 54% in the right ventricle and only 26% in the left one. /1240

Determination of glycogen content in the ventricles of the heart revealed no significant difference between the control and HK animals (4.9 ± 0.4 and 4.7 ± 0.12 mg/g of fresh weight, respectively).

We do not consider that the small reduction in glycogenolysis which we found in both ventricles of the heart, and glycolysis in the right one, plays a decisive role in the reduction of contractile capability of the myocardium and its resistance to anoxia, in animals subjected to the effects of hypokinesia for a period of 30-40 days. It is known from the literature that, as a result of 30-day hypokinesia, a considerable change in the morphological picture is noted in the myocardium, consisting of swelling of the sarcoplasm, accumulation of lipids in it, swelling of the mitochondria and decrease in the number of cristae in them, disruption of the cell membrane structure and lysis of individual myofibrils [8, 9]. A reduction showed up in the oxidative metabolism [7, 8]. All of this undoubtedly plays a significant role in the reduction in efficiency of the myocardium. However, the slowing down of glycolytic metabolism, especially under conditions of disruption of oxidative metabolism, should show up unfavorably on the contractile ability of the heart muscle and its resistance to anoxia. It is not accidental that the change in rate of glycolytic metabolism in various tissues, including the myocardium, always correlated with change in resistance of these tissues to certain unfavorable actions, in all our previous investigations. Thus, in animals adapted to hypoxia, an increased resistance of the brain, myocardium and skeletal muscles was found to various damaging actions. In this case, an increased rate of glycolytic metabolism showed up in all the tissues mentioned [1-3, 12, 13, 16, 17]. On the other hand, after prolonged immobilization of animals, the resistance of the brain and skeletal muscles dropped and the glycolysis rate dropped in parallel with it in these tissues [4, 6]. Apparently, change in efficiency of anaerobic glycolysis actually is one of the components shaping a specific level of resistance of individual tissues and the entire body.

Conclusions

1. A month-long hypokinesia leads to weakening of the contractile capacities of the myocardium of rats and to reduction in its resistance to acute oxygen insufficiency.

2. Simultaneously, a small reduction in anaerobic metabolism rate is noted, which, as we propose, may be one of the components defining a new reduced level of resistance of the heart muscle.

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